Enterocutaneous fistula

Causes and management

Raafat R. Ahmad, *FIBMS (Dig.Surg.), CABS,* ***Shawqi Y. Fawzy,*** *FRCS (Edin), FRCS (Eng).*

ABSTRACT

Objective: To study the main causes of fistula, and to determine the factors related to a successful treatment.

Methods: From November 2002 to October 2005, a total of 70 consecutive patients with enterocutaneous fistula in Gastroenterology and Hepatology Teaching Hospital, Baghdad, Iraq, were studied prospectively. Fifty-two patients received total parenteral nutrition. Internal gastrointestinal fistula, and pure pancreatic and biliary fistula were excluded from this study.

Results: In 68 patients, the fistula developed postoperatively, the most common primary cause was missile injury (42%), and 2 patients have fistula that developed spontaneously. The fistula was healed by conservative treatment in 34 patients, and by surgical intervention in 10. Twenty-five patients died, and in one patient the fistula failed to heal by conservative as well as by surgical treatment. The mean duration of hospital stay for all patients was 25.9 days.

Conclusion: The most common cause of enterocutaneous fistula found in this study was missile injury. Duodenal fistula and, to a lesser extent, ileal fistula, respond more to conservative treatment. High output and jejunal fistula were associated with poorer outcome. Octreotide administration did not significantly improve the output of the fistula or the outcomes.

Saudi Med J 2007; Vol. 28 (9): 1408-1413

From the Department of Surgery (Ahmad), Gastrointestinal and Hepatology Teaching Hospital, and Department of Surgery (Fawzy), Baghdad Medical Collage, Baghdad Teaching Hospital, Medical City, Baghdad, Iraq.

Received 5th February 2007. Accepted 5th May 2007.

Address correspondence and reprint request to: Dr. Raafat R. Ahmad, Department of Surgery, Gastrointestinal and Hepatology Teaching Hospital, PO Box 61103, Bab-Almuaddam, Medical City, Baghdad, Iraq. Tel. +9641 7788126. Fax. +9641 4154642. E-mail: rrahmad2003@yahoo.com

Enterocutaneous fistula (ECF) is a pathological communication between any part of the gastrointestinal tract and skin, which leads to loss of digestive juices that contains water, electrolytes and nutrients. In the past 40 years, the role of malnutrition in enterocutaneous fistula was recognized to be associated with increased morbidity and mortality.[1] This realization was ascertained in a previous study carried out in 1964, that patients with fistula who received more than 3000 kcal/day had a mortality of 12%, whereas those who received less than 1000 kcal/day had a mortality of 55%.[2] Since that time, and as result of introduction of parenteral nutrition (PN) during 1970s, the mortality rate was reduced dramatically, and the incidence of spontaneous closure increased, and if spontaneous closure does not occur because of fistula anatomy, patients often will be in better condition for surgical intervention.[3] This improvement in fistula outcome is not only due to PN, but also due to the advance in the parasurgical care including monitoring, respiratory care, and better fluid and electrolyte balance.[4] However, ECF still have a high unacceptable mortality rate,[5] and their management is a big challenge to the surgeons because it results in serious complications that lead to prolonged hospitalization, and increase the cost of treatment. In addition to that, it causes a big psychological distress to the patients due to severe discomfort, pain, malodorous of drainage fluid, and poor body image. The aim of this study is to review the etiology of ECF, study the outcome of this serious disease, and to determine the factors related to the successful treatment or to the increased mortality and morbidity.

Methods. During a period of 3 years, from November 2002 to October 2005, 70 patients with enterocutaneous fistula in the Gastroenterology and Hepatology Teaching Hospital, Baghdad, Iraq, were studied prospectively. There were 56 males and 14 females, with the mean age of 36.1 years, ranging

between 7 - 75 years. Fifty-four patients were referred from elsewhere for further management due to treatment failure, after a period that varies from one week to 4 months. Each fistula was classified by anatomical location (such as esophageal, gastric, and so on), primary cause (such as missile injury, colorectal carcinoma, and so on), mode of closure (spontaneous or surgical closures), and volume of output (high output: >500 ml/24hour[h], moderate output: 200-500 ml/24h, and low output: <200 ml/24h). We have excluded pure biliary, pancreatic, and internal gastrointestinal fistula from this study because they have different management and prognosis.Fifty-two patients received total parenteral nutrition (TPN), consisting of 0.25-0.30 gm/kg/day(d) nitrogen (1.5-1.8 gm/kg/d protein)[6] as intravenous amino acid (Vamin®, Fresenius Kabi, Germany), and non-protein energy in a ratio of 150 kcal for each one gram of nitrogen given.[7] The total amount of non-protein energy is subdivided into 2/3 as hypertonic glucose water 10 or 20%, and 1/3 as intralipid 10 or 20%.[7] The total amount of energy given to each patient is 40-50 kcal/kg, which constitute 15% amino acid, 25% fat, and 60% glucose. Total fluid given to the patient is calculated by adding fistula output + urine output + insensible fluid loss (500-1000 ml/d), and an addition of 250 ml/d for each 1°C rise in the body temperature. Sodium and chloride is given 1-3 mmol/kg body weight per day as isotonic sodium chloride 0.9%; 1-2 mmol /kg/d of potassium is given, and added 10-30 mmol for each one liter loss from the fistula.[8] A 0.2-0.5 mmol/kg/d of Calcium as calcium gluconate 10%/ampoule, and 0.05-0.1 mmol/kg/d of Magnesium as magnesium sulfate were added to the intravenous fluid, daily. Vitamin B12, vitamin B complex, and vitamin C were added, in appropriate amount. Those patients who received the oral intake were omitted.

The TPN was administered through either peripheral route (cannula placed into cubital fossa veins) for short-term TPN, or a central catheter was placed percutaneously into superior vena cava through internal jugular or subclavian vein for long-term parenteral nutrition. The standard measures were taken to avoid skin irritation. All patients received antibiotics consisting of metronidazol and third generation cephalosporin, or according to the culture and sensitivity results. Baseline body weight, vital signs, and laboratory values were recorded on admission. Vital signs were checked every 8 hours; bedside blood glucose was checked every 4 - 6 hours at the beginning, and once daily thereafter. Fluid balance and body weight was recorded daily. Serum electrolytes including magnesium, liver, and renal functions tests were obtained twice weekly. Abdominal ultrasonography was performed for all patients on admission, and during investigation for fever to discover hidden abscess. Gastrointestinal series and fistulogram was obtained, if the patients do not respond to medical treatment, or when the surgical intervention was decided. Our strategy is to treat all patients conservatively, primarily for 6 weeks, and surgical interventions was only adopted when the fistula do not heal after this period, or when there is an anatomical (intestinal obstruction) or a pathological (malignant fistula) condition prohibit a spontaneous closure.

Student-t-test and chi-squared test were used for the statistical analysis of the parameters between the subgroups. A p value of less than 0.05 is considered the level of significance.

Results. From those 70 patients, in 34 patients (48.5%) the fistula were healed spontaneously by conservative management, with a mean duration of spontaneous closure of 16.6 days, ranging between 3-60 days; in 10 patients (14.2%) the fistula were closed by surgical intervention, 25 patients (35.7%) patients who died, and the main causes of death were related to uncontrolled sepsis, such as multiple organ failure (MOF). One patient with malignant colonic fistula failed to close either by conservative or by surgical treatment. The mean duration of hospitalization of all patients was 25.9 days ranging between 4 - 210 days (**Table 1**). The most common anatomical type of the fistula found in this study was jejunal fistula (25 patients, 35.7%), which has the largest output volume (mean 1600 ml/24h, range between 500-3000 ml/24h) (**Table 1**). Regarding the relationship between the anatomical types of the fistula and the mortality rate, the most frequent mortality rate was also found in jejunal fistula. The duration of spontaneous closure was the least in gastric fistula, and the most in ileal fistula (**Table 1**). Colonic fistula was associated with least frequent mortality rate, and all except in one patient (who had malignant colonic fistula that failed to close by surgical as well as conservative treatment), the fistula closed surgically by proximal defunctioning colostomy. The duodenal fistula had the most frequent spontaneous closure rate, excluding one patient with oesophageal fistula, followed by ileal fistula.

Morbidity and mortality. The most common complication found in this study was central venous catheter infection, which was treated by removal of the catheter. There were 25 (37.7%) patients who died, and the main causes of death were related to uncontrolled sepsis such as MOF, septicemia, renal failure, and pneumonia. This might be because most of those patients (n=20) were referred in poor moribund condition, and even surgical interventions that were performed to these patients (n=7) did not improve the outcome (**Table 2**).

Table 1 - Correlation between anatomical types of the fistula, and the outcome.

Type	No. of patient (%)	Average output volume (ml/24hour) (range)	Spontaneous closure n (%)	Mean duration of spontaneous closure (days)	Surgical closure n (%)	Mortality n (%)
Esophageal	1 (1.4)	200	1 (100)	10	0	0
Gastric	3 (4.2)	633 (400-1000)	1 (33.3)	8	1 (33.3)	1 (33.3)
Duodenal	16 (22.8)	1106 (500-4000)	12 (75)	14.3	0	4 (25)
Jejunal	25 (35.7)	1600 (500-3000)	9 (36)	21.8	1 (4)	15 (60)
Ileal	17 (24.2)	535 (100-1200)	11 (64.7)	16.9	1 (5.8)	5 (29.5)
Colonic	8 (11.4)	233.3 (100-500)	0	-	7 (87.5)	0*
Total	70 (100)	-	34 (48.5)	16.6	10 (14.2)	25 (35.7)*

*Fistula was failed to close either by conservative or by surgical treatment in one patient.

Table 2 - The rate of complications, and the causes of death. (Note: Some patients have more than one complication).

Complications	No. of patients	No. of Mortality
Fistula related		
Renal failure	9	5
MOF	6	6
Septicemia	6	6
Electrolyte disturbance	4	3
Malnourishment	2	1
TPN related		
Hyperglycemia	4	
Central vein infection	13	
Not related		
Pneumonia	3	1
Heart failure	1	2
Bleeding	3	1
Total	51	25

MOF - multiple organ failure, TPN - total parenteral nutrition.

Etiology and outcome. There were 7 main causes of ECF found in this study. Missile injury is the leading cause of fistula (30 patients, 42.8%), in 17 patients (56.6%) the fistula were healed spontaneously, 11 (36.6%) patients died, and in one patient the fistula was closed by surgical intervention, with a mean duration of spontaneous closure of 14 days. The most frequent mortality rate was found in patients who had fistula that developed after the operations for road traffic accident (100%), which might be because of multiple associated injuries. However, fistula following operation for inflammatory bowel disease had the most frequent spontaneous closure rate (80%), but they had the longest mean duration of spontaneous closure (31.5 days). There were only 2 spontaneous fistulas; their primary pathology was recurrent carcinoma of the colon in the first patient, and irradiation for carcinoma of the rectum in the second patient (**Table 3**).

Role of octreotide. If we exclude esophageal and colonic fistula, octreotide (somatostatin analogue) was prescribed for all patients (n=61), but was received by 29 patients only due to the unavailability of the drug most of the time. There was a decrease in fistula output if octreotide is given to duodenal fistula, but this is not statistically significant, and without any effect on jejunal and ileal fistula output. In addition, our study revealed that administration of octreotide with TPN has no significant improvement in spontaneous closure rate; 17/27 (62%) versus 13/23 (25%) [$p>0.05$], or a mortality rate of 9/27 (33.3%) versus 10/25 (40%) [$p>0.05$], if they are compared with patients who received TPN alone (**Table 4**).

Effect of output of the fistula, serum albumin, and hemoglobin on the outcome. This study revealed that the increase in fistula output is associated with a significant rise in the mortality rate. The higher surgical closure rate and the lower spontaneous closure rate found in this study were in low output fistula group, because most of them belong to colonic fistula, which was treated by surgical intervention. On the other hand, this also revealed that there is no statistical significant effect of serum albumin and hemoglobin level on the outcome of the fistula (**Table 5**).

Discussion. The most common primary pathology of postoperative ECF found in this study was missile injury. In reviewing other studies it is found that the most common causes were due to cancer operation, operations for inflammatory bowel disease, and adhesiolysis.[9-12] This could be explained by high incidence of violence because of the wars that the country have went through. Also, there is a relatively low incidence of spontaneous fistula found in the present study, which was only 4% (one case of recurrent colonic and the other, irradiation), as compared to other studies ranges between 15-25%,[2,11-13] and the main causes

Table 3 - The correlation between the etiology of enterocutaneous fistula, and the outcome.

Etiology	No. of patient	Spontaneous closure n (%)	Mean duration of spontaneous closure. Days (range)	Surgical closure n (%)	Mortality n (%)
Missile	30	17 (56.6)	14 (3-36)	2 (6.6)	11 (36.6)
Colorectal cancer	6*	1 (16.6)	10	2 (33.3)	2 (33.3)
Inflammatory bowel disease	5	4 (80)	31.5 (3-60)		1 (20)
Cancer of the pancreas	4	2 (50)	18.5 (10-27)		2 (50)
Biliary reconstruction	4	2 (50)	16.5 (14-19)		2 (50)
Road traffic accident	2	0			2 (100)
Spontaneous fistula	2	1 (50)	4	1 (50)	0
Others	17				

*Fistula from one patient failed for conservative, as well as surgical treatment.

Table 4 - The role of octreotide on the output of enterocutaneous fistula.

Type of fistula	With octreotide			Without octreotide		
	No. of patient	Mean	Range	No. of patient	Mean	Range
Gastric*	2	450	(400-500)	1	1000	
Duodenal*	7	785.7	(500-1000)	9	1355	(500-4000)
Jejunal*	13	1653.8	(500-3000)	12	1541	(500-2500)
Ileal*	7	550	(400-1000)	10	590	(100-1200)
Total	29	859.5	(400-3000)	32	1121.5	(100-4000)

*p> 0.5 not significant.

Table 5 - The effect of fistula output, serum albumin and hemoglobin on the outcome.

Parameters	No. of patient	Spontaneous closure n (%)	Mortality n (%)	Surgical closure n (%)
Output of fistula				
Low output	10	3 (30)	0*	6 (60)*
Moderate output	20	10 (50)	7 (35)	3 (15)
High output	40	20 (50)	18 (45)	2 (5)
p value		>0.05	<0.05	>0.05
Serum albumin				
≤35 gm/l	58	28 (48.2)	22 (37.9)	7 (12)*
>35 gm/l	12	4 (33.3)	4 (33.3)	4 (33.3)
p value		>0.3	>0.5	
Hemoglobin				
<10 gm/dl	43	18 (41.8)	18 (41.8)	6 (13.9)*
>10 gm/dl	27	15 (55.5)	7 (25.9)	5 (18.5)
p value		>0.1	>0.1	

*Fistula on one patient failed for conservative, as well as surgical treatment.

of spontaneous fistula found in these literatures were inflammatory bowel disease, radiotherapy, diverticular disease, ischemic bowel disease, pancreatitis, and gynecological disease.[10-13] In reviewing other studies of ECF after the introduction of TPN from 1970, we found that the spontaneous closure rate ranges between 24-72%,[4,13-15] and the mortality rate of 5-21%.[4,13,16] On the anatomical types of fistula, the result of this study challenge the traditional concept that the ileal fistula had low spontaneous closure rate, and they usually need surgical intervention for closure,[5] but the present study revealed that half of these fistula healed spontaneously, which is a good result as compared with other studies done in Pennsylvania and Texas, which showed that the spontaneous closure rate of ileal fistula were 19%.[4] The reason why all colonic fistulas were treated by surgical intervention (proximal colostomy) is that, those patients had been treated by conservative treatment before referral to our hospital, but without response. Edmund et al[16] found that 92% of colonic fistula were treated by surgical resection or proximal defunctioning colostomy, with low mortality rate and recurrence rate, and assumed that surgical treatment for lower bowel fistula offer an attractive alternative to prolonged medical management. It is well known that the 3 main complications of ECF are sepsis, electrolyte disturbance, and malnutrition.[5] However, electrolyte disturbance and malnutrition became uncommon nowadays, because of good monitoring of nutritional status and electrolyte changes, and because of the introduction of PN. These improvements in complications' incidence were proved in this study, where 8% of the electrolyte disturbance, and 4% malnutrition occur. However, sepsis was the most common cause of death in this study as it is the main cause of multiple organ failure and renal failure, which was also proved by Fazio et al's[17] study. Septicemia occurred in 6 patients (10%) in this study and all of them died. As compared with other studies, septicemia occurred between 9.6% and 62.9%.[18-20] Generalized sepsis usually results from catheter sepsis or pus collection adjacent to fistula tract mainly, but there is another less common causes like pneumonia (due to patient immobility), severe urinary tract infection (from prolong use of indwelling urinary catheter), and wound infection. In addition to that, patient with ECF usually were immunocompromized because of malnutrition, and prolong use of antibiotics. Another common and serious complication is catheter sepsis, which occurred in 13 patients out of the 40, who received central hyperalimentation. This high incidence of central catheter sepsis may be because of the lack of trained staff who can manipulate this special type of catheter aseptically, as a bacterial catheter sepsis is directly related to catheter care.[8] This was proven by a study in the University of Cincinnati Medical Center, where sepsis rate decreases from 27 - 0.6%, after the establishment of a hyperalimentation team and a rigid protocol.[8] Catheter sepsis is suspected if the patient who was previously afebrile, suddenly develops a high fever. Other sources of infection such as pneumonia, intraabdominal abscess, urinary tract infection, and wound infection should be excluded. Initially, the intravenous tube set and the bottle should be changed, and if the fever persists after 8 hours the catheter should be removed, and the tip cultured.[8] The peripheral hyperalimentation may be safer, but it is useful only under limited circumstances, particularly when the duration of PN is expected to be short.

In this study, peripheral hyperalimentation had been used in 21 patients; almost all those patients need to change the cannulla every 1-3 days, due to superficial thrombophlebitis. This method of administration had been used when a short-term PN is expected, or failure to obtain central line, or the central line had been removed when it become infected. Kaushal and Carlson[14] emphasized that, when nursing expertise is limited and in whom the likelihood of spontaneous closure seems high, intravenous feeding using a peripheral sited catheter may be appropriate, and is associated with a low risk of serious morbidity than centrally administered TPN. The results of this study could not show a significant change in healing rate and total volume of fistula output, after administration of octreotide. Spiliotis et al[21] proved that octreotide significantly reduces the output, and accelerate spontaneous closure rate. This was also ascertained by Gonzalez-Pinto and Gonzalez.[10] While Kingsorth et al[22] conclude that somatostatin failed to accelerate closure of ECF in spite of reducing fistula output. Hesse et al[23] reviewed 6 studies that have examined the effect of octreotide on fistula output reduction, where 3 studies showed a significant reduction in fistula output and none showed increased closure rate, but there is a reduction with the time of closure. Arebi and Forbes[13] conclude after reviewing 6 comparative studies and 4 non-comparative studies on effect of octreotide on outcome of ECF, that there is insufficient evidence to recommend the use of somatostatin or its analogues in the management of high-output ECF. In the study by Alvarez et al,[24] octreotide administrations has lead to reduce fistula output, but significantly increase the incidence of septic and thrombotic complications, and failed to affect the fistula duration, spontaneous closure rate, and length of hospitalization. The most important physiological determinant of a fistula is the daily output of the intestinal fluid. Fistula output is often depending on the anatomical site, and high output fistula is more difficult to treat.[10] This study showed that the output

volume is inversely related to spontaneous closure rate, and directly related to the mortality rate. This might be because those patients are complaining of higher incidence of electrolyte disturbance and malnutrition, which associated with more septic complications. Fazio et al[17] found that hypoalbuminemia and anemia is strongly associated with increased mortality rate of ECF. But in our present study, these 2 factors had not been shown to affect the outcome significantly.

The most common cause of ECF found in this study was missile injury. We conclude that even with a good number of patients that was treated successfully in this hospital, there is still a number of unacceptable morbidity and mortality. High output fistula, jejunal fistula, and multiple injuries are associated with highest mortality. Duodenal fistula and, to a lesser extent ileal fistula, are more responding to conservative treatment. Octreotide administration does not significantly improve the output of the fistula or the outcomes, and we recommend future study of surgical management of enterocutaneous fistula.

References

1. Jeejeebhoy KN. Total parenteral nutrition: potion or poison. ***Am J Clin Nutr*** 2001; 74: 160-163.
2. Hollender LF, Meyer C, Avet D, Zeyer B. Postoperative fistulas of the small intestine: therapeutic principles. ***World J Surg*** 1983; 7: 474-480.
3. Falconi M, Pederzoli P. The relevance of gastrointestinal fistulae in clinical practice: a review. ***Gut*** 2001; 49: iv2-iv10.
4. Dudrick SJ, Maharaj AR, McKelvey AA. Artificial nutritional support in patients with gastrointestinal fistula. ***World J Surg*** 1999; 23: 570-576.
5. Fischer JE. The pathophysiology of enterocutaneous fistulas. ***World J Surg*** 1983; 7: 446-450.
6. Anthony Goode. Nutritional support and rehabilitation. In: Mann C, Russell RCG, Williams NS, editors. Bailey &Love's short practice of surgery. London: Chapman & Hall Medical; 1995. p. 43-50.
7. Waitzberg DL, Plopper C, Terra RM. Postoperative total parenteral nutrition. ***World J Surg*** 1999; 23: 560-564.
8. Fischer JE. Metabolism in surgical patients: protein, carbohydrate and fat utilization by oral and parenteral routes. In: Sabiston DC, Lyerly HK, editors. Textbook of surgery: the biological basis of modern surgical practice. Philadelphia: WB Saunders Company; 1997. p. 137-175.
9. Aguirre A, Fischer JE, Welch CE. The role of surgery and hyperalimentation in therapy of gastrointestinal-cutaneous fistulae. ***Ann Surg*** 1974; 180: 393-401.
10. Gonzalez-Pinto I, Gonzalez EM. Optimizing the treatment of upper gastrointestinal fistula. ***Gut*** 2001; 49: iv22-iv31.
11. Soeters PB, Ebeid AM, Fischer JE. Review of 404 patients with gastrointestinal fistulas. Impact of parenteral nutrition. ***Ann Surg*** 1979; 190: 189-202.
12. McIntyre PB, Ritchie JK, Hawley PR, Bartram CI, Lennard-Jones JE. Management of enterocutaneous fistulas: a review of 132 cases. ***Br J Surg*** 1984; 71: 293-296.
13. Arebi M, Forbes A. High-output fistula. ***Clin Colon Rectal Surg*** 2004; 17: 89-97.
14. Kaushal M, Carlson GL. Management of enterocutaneous fistula. ***Clin Colon Rectal Surg*** 2004; 17: 79-88.
15. Rábago LR, Ventosa N, Castro JL, Marco J, Herrera N, Gea F. Endoscopic treatment of postoperative fistulas resistant to conservative management using biological fibrin glue. ***Endoscopy*** 2002; 34: 632-638.
16. Edmunds LH Jr, Williams GM, Welch CE. External fistulas arising from the gastrointestinal tract. ***Ann Surg*** 1960; 152: 445-471.
17. Fazio VW, Coutsoftides T, Steiger E. Factors influencing the outcome of treatment of small bowel fistula. ***World J Surg*** 1983; 7: 481-488.
18. Rose D, Yarborough MF, Canizaro PC, Lowry SF. One hundred and fourteen fistulas of the gastrointestinal tract treated with total parenteral nutrition. ***Surg Gynecol Obstet*** 1986; 163: 345-350.
19. Sitges-Serra A, Jaurrieta E, Sitges-Creus A. Management of postoperative enterocutaneous fistula: the roles of parenteral nutrition and surgery. ***Br J Surg*** 1982; 69: 147-150.
20. Tarazi R, Coutsoftides T, Steiger E, Fazio VW. Gastric and duodenal fistula. ***World J Surg*** 1983; 7: 463-473.
21. Spiliotis J, Briand D, Gouttebel MC, Astre C, Louer B, Saint-Aubert B, et al. Treatment of fistulas of gastrointestinal tract with total parenteral nutrition and octreotide in patients with carcinoma. ***Surg Gynecol Obstet*** 1993; 176: 575-580.
22. Kingsnorth AN, Moss JG, Small WP. Failure of somatostatin to accelerate closure of enterocutaneous fistulas in patients receiving total parenteral nutrition. ***Lancet*** 1986; 1: 1271.
23. Hesse U, Ysebaert D, de Hemptinne B. Role of somatostatin-14 and its analogues in the management of gastrointestinal fistulae: clinical data. ***Gut*** 2001; 49: iv11-iv21.
24. Alvarez C, McFadden DW, Reber HA. Complicated enterocutaneous fistulas: failure of octreotide to improve healing. ***World J Surg*** 2000; 24: 533-538.